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Training HBCU Faculty and Students in Prostate Cancer (PC)
Research: Signal Transduction and Receptor-Inhibitor
Interactions in the Progress of PC

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14. ABSTRACT This program aims to help eradicate prostate cancer (PC) disparity in African Americans through educational and research programs. Our hypothesis is that through PC education and participation in PC research, a meaningful number of African Americans will be able to contribute to the elimination of disparity in PC. Our program comprises three Specific Aims. (1) To develop, promote, and sustain independent, competitive research and training programs at Xavier University. Both projects are moving forward, presenting data and involving students. (2) To increase the number of Xavier University investigators focused on PC research. One new project has been developed and is involving students. (3) To establish a long-term collaborative relationship between Xavier University and the TCC in PC research. XU faculty in the program are now members of the Tulane Cancer Center and involved in weekly seminars and focus group meetings.					
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3rd Annual Report on Grant #W81XWH-04-1-0252

March 1, 2006 through February 28, 2007

Training HBCU Faculty and Students in Prostate Cancer (PC) Research: Signal Transduction and Receptor-Inhibitor Interactions in the Progress of PC

Thomas E. Wiese, Ph.D.

INTRODUCTION

We intend to help eradicate prostate cancer (PC) disparity in African Americans by targeting this population through educational and research programs. Our hypothesis is that through PC education, exposure to PC issues, and participation in PC research, a meaningful number of African Americans will acquire the knowledge to contribute to the elimination of disparity in PC. Our program comprises three Specific Aims. The first Aim develops, promotes, and sustains independent, competitive research and training programs at Xavier University. This Specific Aim is proceeding on track with both major research projects generating enough data to present at research symposia and both involving students. The second Aim increases the number of Xavier University investigators focused on PC research, to date one Xavier faculty has been matched with an experienced researcher from the Tulane Cancer Center (TCC) and their project is underway and involves Xavier students. The third Aim establishes a long-term collaborative relationship between Xavier University and the TCC in PC research. Xavier faculty involved in this DOD funded PC program are part of a nucleus of Xavier faculty that are now members of the Tulane Cancer Center and involved in weekly seminars and research groups. The most important thing impacting this program in Y3 was the award of an additional funded year to make up for time lost due to Katrina evacuation and rebuilding. This extra year was requested, received and now the program will extend through Feb 2008. In addition, since 2005, the Xavier and Tulane faculty involved in this DOD program are also developing additional cancer research and education programs with the Tulane Cancer Center and the Louisiana Cancer Research Consortium (LCRC). The primary mechanism for this expanded interaction is an NCI P20 planning grant awarded to Xavier and Tulane in October 2005 to develop additional collaborative research projects, a cancer biology course focused on health disparities for students at Xavier and Tulane, cancer research experiences for Xavier students and mechanisms to integrate health disparities education into the professional curriculums at Xavier and Tulane. Dr. Wiese, the PI of this DOD PC program is the Xavier manager of the NCI P20 grant and Dr. Ireland (Xaver Biology) submitted and was awarded a pilot project in the P20 program in 2006. This NCI program is now fully underway along with this DOD program and the Xavier and Tulane DOD Breast Cancer Program (2004-2009).

BODY

This reports funding period covers March 1, 2006 through February 28, 2007.

The impact of Hurricane Katrina on this project has been described in the Y2 progress report. This years update on the recovery effort is that both original projects in the program returned to normal operation by September 2006 when both the emergency, make up semester in summer 2006 was completed and the effected labs came back to full operation. While the Katrina evacuation and recovery was a little more than 4 months, the impact on productivity in research labs at this institution that also had to make up for a lost semester has been considerably more than 4 months. Once labs were in operation in early 2006, then time was needed to validate experiments done prior to the storm and train new people as needed.

Taken together, the significant impact of Katrina on the program involved the loss of laboratory supplies, research personnel and time. However, DOD did award an additional funded year to this project in 2006 and we feel that Katrina impacts have been reduced as much as possible and that project aims can be achieved over the new total funding period.

SPECIFIC AIM I

Develop, promote, and sustain independent, competitive research and training programs at

Xavier University.

A. Ireland/Abdel-Mageed project: “Genetic Basis of Prostate Cancer: Factors influencing the mortality rates of minorities”

1. Search for a replacement technician to assist in project (Months 1- 4)

Dr. Qiuyun Yang did not return to New Orleans after Katrina. After conducting nationwide search, Dr. Padma Sankar was hired in summer 2006 as a replacement.

2. Identify new student(s) to assist in project (Month 3)

Two new students (Ms. Brittany Burton and Ms. Nazima Yousuf) were identified to work on the project since others had graduated.

3. Establish a connection between androgen-receptor presence and activity, and drug resistance (Months 1-9)

a. Establish prostate cancer cell lines (Month 1)

Dr. Ireland has re-established three prostate cancer (CaP) cell lines at Xavier University's cell culture facility. They include PC-3, DU-145 (both androgen independent) and LNCaP (androgen dependent). These cells were lost during the Katrina evacuation and all cell culture capacity in the Ireland lab was re-established in Summer 2006.

b. Test the effect of radiation and chemotherapy on apoptosis (Months 2-5)

(See I.A.4)

c. Test the effect of radiation and chemotherapy on growth (Months 6-9)

(See I.A.4)

4. Identify the relation between NF- κ B and p53 in establishing drug-resistance phenotype in CaP cells (Months 10-21).

To identify the relationship between NF- κ B (a transcription factor and an antiapoptotic agent) and p53 (also a transcription factor and apoptotic tumor suppressor gene), the NF- κ B luciferase reporter assays were conducted in both DU-145 and PC-3 cell lines. While NF- κ B is constitutively activated in both cell lines, PC-3 cells are p53-deficient whereas DU-145 express mutant p53. Hence the assay was designed to determine the possible effects of exogenous, wild-type p53 on NF- κ B. To accomplish this, CaP cells were co-transfected with appropriate plasmids (the control CMV plasmid, the NF- κ B-luc plasmid and the p53 wild type plasmids) and the assays were conducted in presence and in the absence of TNF- α , known inducer of endogenous NF- κ B and wild type adenovirus or I κ B super-repressor adenoviral vector, an inhibitor of NF- κ B activation. Additional transfections and assays were performed in LNCaP cells in presence of CBP/p300 (coactivator for p53 dependent transactivation and repression). Using the luciferase reporter assays, the NF- κ B activation was measured by a fluorometer relative to the normalized levels of endogenous beta-galactosidase activity in each cell line. The results demonstrated that the wild-type p53 inhibits NF- κ B activation by an average of 40 % in the absence of TNF- α , the endogenous NF- κ B inducer. In the presence of TNF- α , this inhibition increased to more than 50 %. These observations were confirmed by Western blot and gel shift analyses.

a. Measure p53 in sensitive and resistant cell lines and PC tissues from biracial populations (Months 10-15).

This aim has been delayed by 6-12 months due to Katrina

b. Measure NF- κ B in sensitive and resistant cell lines and PC tissues from biracial populations (Months 10-15)

This aim has been delayed by 6-12 months due to Katrina.

c. Measurement of NF- κ B-induced expression of anti-apoptotic proteins (Months 16-21)

5. Test if chemoresistance is mediated via crosstalk between NF- κ B and p53 (Months 22-36)

When the luciferase reporter assays were conducted in the presence of wild type adenovirus or adenoviral vector, the results showed that the p53 inhibition of NF- κ B increased by more than 10 fold in PC-3 and DU-145 cells. These observations in PC-3 and DU-145 cells were confirmed by Western blot analyses. In LNCaP cells (androgen receptor positive with mutated p53), the above-mentioned inhibitors actually lost their inhibitory effect on NF- κ B.

These observations suggest that androgen receptor may be involved in modulating the I κ B super-repressor adenoviral inhibitory function. Reproducible results showed that NF- κ B inhibits p53 in PC-3 and DU-145 cells. Results from additional assays conducted in presence of CBP/p300 (coactivator for p53 dependent transactivation and repression) suggest that this coactivator is involved in the mutual inhibitory effects of NF- κ B and p53 in prostate cancer cells.

- a. *Test p53 level and activity after blocking NF- κ B (Months 22-27)*
- b. *Test p53 level and activity after activating NF- κ B. (Months 28-30)*
- c. *Test if changes in NF- κ B status affect p53 status in PC cell lines. (Months 31-36)*

6. Deliverables/measurable outcomes: Dr. Ireland will prepare or oversee the following:

- a. *Semiannual reports will be submitted to the Co-PI*

Dr. Ireland has submitted one report in Y2.

- b. *One abstract will be submitted to a professional conference each year (Months 12, 24, 36)*

Data was presented at the 10th Biennial ICC Symposium on Cancer and Minorities, in Washington DC (April 2006).

- c. *Students involved in the research will present a poster at the annual research workshop (Months 12, 24, 36)*

The schedule of the two new students allowed them little time in the lab which was spent in the training and repeating the previous experiments (for reproducibility). They will present in the next few months at a regional or national meeting.

- d. *One competitive grant application will be submitted by end of Month 24*

Plans are unchanged.

- e. *One paper will be submitted by end of Month 36*

One manuscript is in preparation and is expected to be submitted shortly.

Long-term Impact of Katrina on the overall goals of this project

The goals of this project remain unchanged but due to the extensive loss of lab supplies, loss of time, personnel and data, an extension on the grant will be most helpful. The laboratory has lost officially an entire semester (September through mid-January) but even though the institutions were opened for business mid-January 2006, it has taken more than one year to get it set up again. It has also taken several months to hire a replacement. All cell lines had to be reestablished, all experiments from previous year had to be repeated and therefore an extension will be very helpful for this project.

B. Stevens/Jones project: “The Search for Tyrosine Kinase Inhibitors (TKIs) of Prostate Cancer Cell Growth”

1. Hire technician to assist in project (Month 1)

Tracy Kirksey was hired within one month of initiating this project. She has a B.S. degree in Chemistry from Xavier University. Her primary responsibilities are (1) to grow and maintain the prostate cancer cell lines and (2) to test compounds as prospective inhibitors of ErbB2 tyrosine kinase activity. Because Dr. Stevens has just been elected chair of the Department of Chemistry at Xavier University, she plans to hire another technician to work alongside Ms. Kirksey, performing the molecular modeling studies.

Tracy Kirksey did not return to Xavier after Hurricane Katrina. Ping Jin was hired as a Research Associate in May 2005 to work on the molecular modeling portion of this project (CV included as Appendix #3 in year 2 progress report). Her responsibilities include database mining, building a homology model of the tyrosine kinase enzyme, and docking potential inhibitors.

2. Identify student to assist in project (Month 3)

Joseen Bryant, a chemistry major, was hired within one month of the start of this project. Her primary responsibilities are to use the SYBYL molecular modeling software package to develop a pharmacophore that can be

used to search databases for new compounds to be tested for tyrosine kinase inhibition. Dr. Stevens is adding three additional students to this project. The first, Nicole Bell, is a Graduate Alliance for Education in Louisiana (GAELA)/American Chemical Society Scholar. She has already contributed significantly to this project, solving the two x-ray crystal structures described in Aim I.B.3. Ms. Bell will be supported in part as a Slayton Evans Summer Research Scholar. The other two students are Nyote Oliver, who is a MARC Scholar, and Shelley Schmidt.

Joseen Bryant did not return to Xavier after Hurricane Katrina. Nicole Bell has continued to work on the crystal structures of tyrosine kinase inhibitors. A senior, Aviva Baird, has joined the group and will begin working on the CoMFA study.

March 2007 - Both Nicole and Aviva graduated from Xavier. Both are attending graduate school in the chemical sciences. Torrey Fingal was hired in November 2006 to work on this project. He has been trained in x-ray crystallography and will begin working on the molecular modeling component this summer. Peter Tran, a MARC scholar, has also joined the group and has been working on the x-ray crystallography.

3. Identify novel small molecules that inhibit ErbB2 activity related to among quinazoline, pyrimidine, and quinoline derivatives (Months 1-18)

a. Determine X-ray crystal structures of known tyrosine kinase inhibitors (quinazoline, pyrimidine, and quinoline derivatives) (Months 1-12)

The x-ray crystal structures of a third tyrosine kinase inhibitor has been completed. This is N-(3',4'-dihydroxybenzylidenecyanoacetyl)indoline, a tyrphostin derivative. Crystals were obtained by slow evaporation of solvent and x-ray diffraction data were collected at room temperature on an Enraf-Nonius CAD4 diffractometer with a molybdenum target x-ray tube. Data were refined on a LINUX workstation with the maXus software package (Bruker Instruments). The structures are included as Appendix A-4 in the year 1 progress report. The Stevens group continues to recrystallize available tyrosine kinase inhibitors. As crystals are obtained, they will collect x-ray diffraction data for these compounds. These x-ray crystal structures will be used as reference structures for the molecular modeling results.

March 2007 - Three more x-ray crystal structures of 4-methoxybenzylidenemalononitrile, α -cyano-(3,5-di-*t*-butyl-4-hydroxy)thiocinnamide, and 4-[(3-bromophenyl)amino]-6-propionylamidoquinazoline have been completed. We continue to crystallize samples of tyrosine kinase inhibitors.

b. Identify detailed pharmacophore and determine geometric, electronic, and lipophilic characteristics required for tyrosine kinase inhibition using

Comparative Molecular Field Analysis quantitative structure activity relationships (Months 1-12)

An extensive literature search was used to identify small molecules that are known to inhibit ErbB2 activity. These molecules are related to quinazolines, pyrimidines, quinolines, and tyrphostins. Dr. Stevens has collected a library of molecules that have been divided into two sets. One set includes 31 tyrphostins whose EGFR and ErbB2 activities were measured by Gazit and Levitzki.¹⁻³ The second set includes 71 quinazolines and similar molecules whose activities were measured by Wissner.⁴⁻⁶

Using the molecules with known activity against prostate cancers cell lines, a third pharmacophore model has been developed (see Appendix A-5 in year 1 progress report). This pharmacophore model along with the two that had been developed last year identify the geometric relationship between structural features of a set of molecules known to act as tyrosine kinase inhibitors.

c. Identify new compounds to be tested for tyrosine kinase inhibition with conformationally flexible searches of compound databases using detailed pharmacophore and CoMFA QSAR results (Months 9-18)

The geometric models noted in I.A.3.b have been used to search databases for new compounds having the same geometric arrangement of structural features but not yet been identified as tyrosine kinase inhibitors. These databases have been installed and are available for searching at Xavier University. They include the Available Compounds Database (Molecular Design Limited), the National Cancer Institute Database, the EPA Toxic Chemicals Database, and the SMILE CAS Database. Software available for database searching includes HiVol and Unity (part of the SYBYL software package).

Preliminary searches with successive filtering yielded several hundred prospective compounds. Additional virtual compound screening by docking these compounds into a homology model of the receptor is planned. A Comparative Molecular Field Analysis (CoMFA) QSAR study of the quinazoline derivatives has begun. Because of delays imposed by Hurricane Katrina, Dr. Stevens plans to complete this study by August 2006. The database has been created with nearly 80 molecules. The structures of all molecules have been optimized and MOPAC charges have been calculated. The most difficult part of the study has been to obtain an appropriate alignment of all molecules in the database. Dr. Stevens plans to begin the database search using the pharmacophore models developed during the past year. At that point, she will use the CoMFA model results to search for additional compounds that might be active as tyrosine kinase inhibitors.

4. Explore the mechanism of ErbB2 tyrosine kinase inhibition (Months 13-24).

Plans are unchanged.

a. Build a homology model of the ErbB2 tyrosine kinase ATP binding site.

(Months 13-18) March 2006 - Dr. Stevens' group has begun learning how to build homology models using the Composer module in SYBYL 7.1. They have used this software package to build a homology model of P450 2B1 using the protein crystal structures of P450 2B4 as templates with the sequence of P450 2B1 used as the target. The initial model was refined and submitted to a series of tests to determine its quality and consistency using Procheck and ProsaII.

March 2007 - A homology model of ErbB2 was built based on three protein crystal structures (Epidermal Growth Factor Kinase Domain (1M14), Epidermal Growth Factor Receptor Kinase Domain with bound erlotinib (TercevaTM) (1M17), and Epidermal Growth Factor Receptor Kinase Domain with bound GW572016 (LapatinibTM) (1XKK)) which are available from the Protein Data Bank. The sequence of human ErbB2 was obtained from the SwissProt database and was used as the target. The Composer module in SYBYL 7.1 was used to construct the three-dimensional model of ErbB2. The initial model was refined by minimizations carried out by the 2000 steps of steepest descent method followed by the conjugate gradient method until the root mean square gradient of the potential energy was < 0.05 kcal/mol Å. The minimized homology model was validated using Procheck and ProsaII. The results showed that our homology model is consistent with a good quality structure comparable to a high resolution X-ray structure.

b. Dock proven and proposed TKIs into the tyrosine kinase ATP binding site using multiple poses, and score results (Months 18-24)

March 2007 - The program GOLD (Version 3.1.1) from the Cambridge Crystallographic Data Center was used to dock the tyrosine kinase inhibitor candidates (obtained from our UNITY search of databases using the quinazoline pharmacophore model) into the ATP site of ErbB2 for virtual screening. GOLD is an automatic docking program that uses a genetic algorithm for docking flexible ligands into protein binding sites. The three times speed-up was chosen as a Genetic Algorithm Parameter. Chemscore was chosen as the scoring function. The Chemscore parameter file was edited to include a Kinase score function and validated to ensure that it has the power to discriminate between the promising TKI candidates and the unpromising candidates. The docking was repeated five times to avoid the stochastic nature of the docking algorithm. The five docking runs resulted in approximately 100 molecules which will be submitted for tests of activity in prostate cancer cell lines.

5. Determine activity and specificity of novel ErbB2-targeting molecules; specifically, the ability of each small molecule to ablate ErbB2 activation (Months 18-36)

Plans are unchanged.

6. Determine the impact of novel ErbB2-targeting molecules on PC cell growth; specifically, determine the effect of the ErbB2 inhibitor on the growth of LNCaP-ErbB2 cells using several standard cellular growth assays. (Months 18-36)

Plans are unchanged.

7. Deliverables/measurable outcomes: Dr. Stevens will prepare or oversee the following:

a. Semiannual reports will be submitted to the Co-PI

Dr. Stevens has submitted semiannual reports to the coPI.

- b. *One abstract will be submitted to a professional conference each year (Months 12, 24, 36)*

No off-campus presentations have yet been made by Dr. Stevens. Her generation of computational data and of completed x-ray crystal structures, however, leaves little doubt that significant publishable progress has been made. Unfortunately, Hurricane Katrina interrupted the momentum associated with presenting results at scientific meetings. Being displaced in Virginia from September – December 2006 meant that abstracts planned for the American Crystallographic Association, American Chemical Society, and American Association of Cancer Research could not be submitted.

Dr. Stevens was invited to present a seminar on her research at Towson University (Nov. 2006) as part of their seminar series. She presented a seminar that included results from this research project “Structural Studies of Inhibitors of Cancer Initiation and Growth”.

- c. *Students involved in the research will present a poster at the annual research workshop (Months 12, 24, 36)*

Dr. Stevens’ research student, Nicole Bell, has already presented her work at the American Chemical Society meeting in August 2005. These presentations included the following:

- Nicole M. Bell, Naijue Zhu, and Cheryl L. Klein Stevens, “A Crystallographic Study of ErbB2 Tyrosine Kinase Inhibitors”, 230th American Chemical Society National Meeting, Washington, DC, August 2005.

Peter Tran presented a poster at the American Chemical Society meeting in March 2007.

- Peter Tran, Naijue Zhu, and Cheryl L. Klein Stevens, “X-ray Crystal Structures of ErbB2 Tyrosine Kinase Inhibitors (TKIs)”, 233rd American Chemical Society National Meeting, Chicago, IL 2007.

- d. *One competitive grant application will be submitted by end of Month 24*

Plans are unchanged.

- e. *One paper will be submitted by end of Month 36*

Plans are unchanged.

SPECIFIC AIM II

Increase number of Xavier University investigators focused on PC research.

A. The Co-Project Director will identify two additional Junior Faculty that express an interest in PC research in order to include them in the group activities (Month 1)

One Xavier University faculty member, Dr. Gurdial Arora of the Department of Mathematics, was partnered in 2005 with Dr. Suresh Sikka, a Tulane Cancer Center prostate cancer researcher. Dr. Arora is using his expertise in statistics to analyze data collected by Dr. Sikka. Xavier students are learning techniques in the Sikka lab while gaining exposure to prostate cancer research. This project has developed as described below.

In January 2007, Dr. Duane E. Johnson was hired in the Division of Basic Pharmaceutical Sciences in the Xavier College of Pharmacy. Dr. Johnson was previously a professor at Dillard University in New Orleans and lost his job with Katrina related downsizing. When Xavier Pharmacy advertised for a pharmacology position in Fall 2006, Dr. Johnson applied. One of the key aspects to developing his interest in Xavier was the Cancer Research programs at Xavier, specifically the chance to join one of the DOD programs. Dr. Johnson brought with him a Komen Foundation cancer research grant and is eager to further develop this and other health disparities related projects at Xavier. The CV and Research interests statement from Dr. Johnson are in Appendix 2. We are excited about Dr. Johnson joining our cancer research group and look forward to utilizing the DOD programs to assist in the development of his projects.

Title: Development of Biomarker for Early Detection and Prevention of Benign and Malignant Prostate Disease in Aging Men

**Gurdial Arora, Ph.D. - Xavier University, New Orleans, LA, and
Suresh C. Sikka, Ph.D., HCLD – Tulane University Health Sciences Center, New Orleans,**

Hypothesis: Certain biomarkers involved in specific cellular and molecular mechanisms express selective gene mutations due to altered oxidative stress in the aging prostate. Early detection of such biomarkers may help in our understanding of biology of benign and malignant prostate cancer development and in designing ways to prevent or treat this disease in early stage.

Goals: Our overall goal is to identify such potential biomarkers and selective genes influenced by oxidative stress using *in vivo* and *in vitro* approaches, characterize them by mathematical models, and investigate their association with clinical benign and malignant prostate cancer development and prevention.

Introduction: As men age, environment, diet, and genetics play a significant role in the development of benign prostatic hyperplasia (BPH) or prostate cancer (PC). How these etiologic factors interact in prostate growth and differentiation leading to cancer is not fully known. Altered redox mechanisms affecting cellular oxidative insult leading to specific gene mutations is now considered to be a key hypothesis in this respect. Oxidative insult or stress is a condition caused by increased generation of free radicals and/or decreased antioxidant capacity in associated cells and tissues. By far, the preventative and early therapeutic options available to men prone to BPH and/or PC are limited - mainly due to the lack of markers for early detection of these conditions. In addition, there is no clear understanding of cellular and molecular mechanisms that are responsible for genetic mutations due to altered oxidative stress in the aging prostate.

Specific Aims and Progress:

1) ***Oxidative stress and prostate growth:*** Dr. Sikka in his laboratory at Tulane recently demonstrated a differential growth and inhibition pattern in benign and normal prostate epithelial cells in response to oxidative insult. BPH cells, unlike normal prostate cells, showed significant proliferative response over control under very low oxidative stress. By induction of apoptotic stimuli (investigated by caspase activation), this selective BPH proliferation could be prevented by antioxidants (vitamin E and selenium). Dr. Sikka hypothesizes that low oxidative stress is responsible for inducing genetic and physiological events in cells most prone to such altered responses.

2) ***Calcium channels as Biomarkers:*** In this context Dr. Sikka has observed that intracellular calcium ($[Ca^{2+}]_i$) plays a vital role that may regulate the differential growth patterns that exists between BPH and normal prostate epithelial cells under conditions of induced oxidative stress. The mRNA expression of T-type Ca^{2+} channel was observed only in BPH cells at low oxidative stress (even near the resting membrane potential) resulting in the elevation of basal $[Ca^{2+}]_i$ concentration. Dr. Sikka is currently evaluating other specific $[Ca^{2+}]$ channels in normal and cancer cells. In addition, the preliminary results have shown that the expression levels of gene and/or protein of cytochrome c oxidase II and III subunits are extremely low in BPH cells but relatively higher in normal prostate epithelial cells. Since the mitochondrial potential and activities of such key redox enzymes play an important role in activation of caspase cascade leading to induction of apoptosis, Dr. Sikka plans to evaluate the expression of these subunits II, III at both gene and protein levels. Dr. Sikka hypothesizes that this differential response is due to induction of specific mutations and/or deletions in these key mitochondrial enzymes. Evaluation of such mutations/deletions with functional expression of selective calcium channels can be used as biomarkers for early detection and prevention of benign and malignant prostate disease in aging men. We plan to specifically use the patient resources (biopsy tissue, EPS and blood samples) from men of various age groups who attend Tulane Urology clinics and focus on evaluating these biomarkers.

3) ***Mathematical Modeling of Biomarkers Expression:*** Dr. Arora's participation related to this project is multifold. First he will learn the terminology and specific problems (epidemiological, pathophysiological, genetic linking, early diagnosis, prevention and treatment) related to this area, which are of paramount importance. He will also use his expertise in the area of mathematical modeling and applied bio-statistics to analyze the data so far generated by Dr. Sikka's research in this area. He will use the software SPSS to analyze the data and statistical and mathematical techniques to model the problems. The students will also learn to use the software SPSS and relevant statistical and mathematical techniques. The goal is to collaborate with Dr. Sikka's group on this project, learn from their expertise and hope to continue working with Dr. Sikka and submit grant for funding in the near future.

During summer of 2005, one Xavier student Miss S. Grahams worked on this project. She met Dr. Sikka two times in his lab at Tulane Medical School to observe cell culture work. Miss Grahams was full of enthusiasm to work under the guidance of Dr. Sikka. This was a great opportunity to get introduced to this new exciting field. We were in the process of entering data generated by Dr. Sikka into the Microsoft excel worksheet but hurricane Katrina hit

our area in August 2005. The data that we entered was on the hard drive which we lost due to hurricane Katrina. The student who was working on this grant decided not to come back to Xavier University. That was bad news for such exciting collaboration between Dr. Arora of Xavier and Dr. Sikka of Tulane Universities.

Further Progress and Plans: After hurricane Katrina, since August 2006, Dr. Arora has been in constant touch with Dr. Sikka to reestablish the collaboration. Dr. Sikka then provided Dr. Arora some current literature in the area of prostate cancer. Two Xavier students, Brittney Richardson and Jocelyn Hooks, with good data analysis skills have now shown their interest in continuing in this collaborative project. These students have already had eight visits to the Tulane laboratories. During those visits, they had the opportunities to work closely with Dr. Sikka and his staff, learning about various aspects of research and cell culture. They have been exposed to new cell culture technology and use of some equipment such as the spectrophotometer, hemocytometer, ELISA plate reader, etc. They have learnt many biological and cell-culture terminology such as cellular confluency, cell proliferation and toxicity, in vitro & in vivo approaches, apoptosis, cell signaling, etc. as a result of being in these research facilities. The students have been active in a recent study involving cell proliferation inhibition, cytotoxicity, and optical density. In this study, LnCap and C4-2B prostate cancer cells were used with the Cell Counting Kit 8 (CCK-8). The students observed cell proliferation cytotoxicity procedures using this kit, and in the process, learned about the use of trypsin to detach cells from cell culture flasks after incubation. They were also introduced to different media that are used to grow such cells. These students were also introduced to the process and significance of a luciferase assay and the polymerase chain reaction (PCR).

In addition to developing their knowledge about research, Brittney and Jocelyn, have also had the chance to use and develop their skills in Microsoft Excel. They have been involved in data input for studies by Dr. Sikka. These experiences have been exciting and motivating for the students. They anticipate the continuation of their learning experience through further involvement in research opportunities.

An NCI P20 Cancer Research and Education Planning Grant under DOD Cancer Training Partnership Grants was submitted for Tulane-Xavier Cancer initiative based upon such collaboration. This competitive grant good recommendation but was not funded. As soon as we will finish analyzing some more data, we plan to submit an abstract and a manuscript and expand the work in order to submit an NCI-extramural grant.

It is a great opportunity to advance our student's training skills and venture into a long standing collaboration between the two institutions in this post-Katrina era. These students also interact with Drs. Ireland of Xavier University and Dr. Mageed of Tulane University and their staff and students at certain lab meetings at Tulane whenever suitable.

B. Establish participation of the selected Junior Faculty in Tulane Cancer Center

The program PI, Dr. Wiese, is informed of and otherwise identifies cancer research seminars at the Tulane Cancer Center and at other universities in the city (LSU Health Sciences and University of New Orleans). Then, Dr. Wiese uses email to notify faculty involved in the DOD programs at Xavier and set up car pooling to attend. Someone from this group has attended most bi-weekly cancer center seminars and most faculty have attended at least one every few months. Attending these TCC seminars has become a regular event for the Xavier faculty involved in cancer research. The tradition from recent years of alternating the sponsor and location of the cancer seminars between Tulane and LSU Health Sciences continues. Attempts to have Xavier cancer researchers invite speakers in to give seminars At Xavier has not been successful. We will try to revive this effort. The main obstacle is that the Xavier faculty involved in cancer research are not willing or able to identify a suitable speaker and then the schedules of these faculty and students prevents solid enthusiasm for the idea. If the Biology, Chemistry and College of Pharmacy at Xavier, only Chemistry has an established seminar time. The chemistry seminars are held on Thursdays at noon, the same time as the LCRC cancer seminars at Tulane and LSU. Xavier cancer research faculty were included as attendees in the Tulane Cancer Center Mauvernay Research Excellence Award Seminar & Poster session held in November 2006.

C. Subscribe to cancer- and/or prostate-related journals (Month 1)

All participants in the program were asked in Y2 what journals they need access to and with recent expansions of the Tulane and Xavier electronic library collections, no deficiencies were identified. It should be noted that the Xavier faculty involved in this project have access to the Tulane library resources that augment the constantly increasing Xavier library collection.

D. Establish information-flow from the Office of Sponsored Programs about funding opportunities in PC (Month 9)

Xavier University's Senior Vice President for Resource Development, who heads the university's Office of Sponsored Programs, regularly forwards information about new funding opportunities to the PI, who passes it on as appropriate to the Xavier University researchers. The Xavier Office of sponsored Programs offers information and training sessions each fall regarding the identification of grants, process for application and procedures for processing applications within Xavier. Xavier retains multiple grant consultants for faculty to use to discuss grants ideas, grant development as well as for the purpose of pre-review of grants.

E. Determine Tulane Cancer Center mentors for the Junior Faculty (Month 6)

See section II.A. above.

F. Junior Faculty collect preliminary data (Months 7-24)

The new research partnership between Drs. Arora of Xavier University and Sikka of the TCC) has developed a budget and account to fund students and purchase supplies and equipment.

G. Host a workshop on grant preparation and how to identify proper funding opportunities (Month 24)

Xavier faculty involved in this project have been working with their mentors and the Xavier office of Sponsored programs to identify suitable funding opportunities. The program PI has also informed participating faculty about local or regional grant writing workshops. No faculty have yet attended these workshops.

H. Junior Faculty develop grant proposal (Months 25-36)

Plans are unchanged. Dr. Arora and Sikka submitted a pilot project proposal for the Xavier –Tulane NCI P20 program in 2006. This proposal was not funded due to fact that they wanted to establish a student training program and P20 program as looking for research. The program PI and others involved in the P20 program have worked with Drs. Arora and Sikka to identify an appropriate funding mechanism.

SPECIFIC AIM III

Establish long-term collaborative relationship between Xavier University and Tulane University Cancer Center.

A. Grant membership in the Tulane Cancer Center to Xavier University researchers including Junior Faculty (Month 1)

All 3 Xavier faculty involved in this program have either been approved as adjunct faculty at Tulane or this approval is pending. Once approved, this status allows Xavier faculty to be contributing members of the Tulane Cancer Center (TCC) as well as the Louisiana Cancer Research Consortium (LCRC). As members, these faculty can use the various core facilities at the cancer center at a reduced rate. To date, all Tulane mentors have facilitated the use of any needed cancer center cores with or without membership. This adjunct status also allows the Xavier faculty doing cancer research to use the Tulane library resources.

B. Include Xavier University researchers (including Junior Faculty) in the Tulane Cancer Center programs/working groups/task forces, which focus on a particular organ such as the prostate or on a specific class of phenomena such as signal transduction (Months 1, 7)

All faculty involved in the Xavier DOD Cancer programs are now integrated into the Molecular Signaling focal group of the LCRC. These faculty are exposed to a wide range of cancer research by attending the Molecular Signaling research meetings. In addition, these faculty are now involved in building stronger ties between Xavier and the LCRC. We have established a monthly Cancer Research lunch meeting at Xavier (see III H below).

C. Include Xavier University researchers (including Junior Faculty) in the Tulane Cancer Center PC journal club (Month 1)

Tulane no longer has a Prostate cancer journal club. However, Xavier faculty doing cancer research are now included in and can present at the Molecular Signaling research meetings of the LCRC (See section III G below).

D. Grant access to core research facilities at the Tulane Cancer Center (Month 1)

Both Drs. Ireland and Stevens share resources in their Tulane mentor's labs. In addition, now that both are members

of the TCC and LCRC, they can initiate use of the various cancer center core facilities. These projects have not yet required resources in the LCRC core facilities.

E. Establish external advisory board (LSU-Tulane Cancer Research Consortium) for the purpose of reviewing program progress, offering solutions to identified problems, and providing an ongoing mechanism for planning improved collaboration (Month 3, 12, 24, 36)

No formal external advisory board has been established. However, the Xavier faculty doing projects in this program interact closely with their mentors and Dr. Wiese, the program PI interacts weekly with Dr. Steven Hill, Program Director and Dr. Roy Weiner, Director of the Tulane Cancer Center. These meetings have formed a very good working relationship that readily formulates solutions to problems that have come up.

F. Invite Tulane University researchers to give seminars at Xavier University (Months 3, 7, 15, 19, 27, 31)

Cancer related seminars at Xavier planned for fall 2005 and Spring 2006 were canceled. The group has not settled on when these will be restarted, but they will likely to start in first quarter 2007.

G. Invite Xavier University faculty-at-large to attend seminars related to PC research (Months 3, 7, 15, 19, 27, 31)

An effort has been made by Dr. Wiese to inform all faculty in the Chemistry and Biology departments as well as all faculty in the College of Pharmacy about cancer related seminars in the city. These faculty are well informed about any cancer research seminars that will take place at Xavier.

It should be noted that Xavier cancer research faculty are informed about and encouraged to attend all the cancer related seminars and working groups in the LCRC. The LCRC invited speaker series is every other Thursday at noon alternating between Tulane and LSU. Other LCRC discussion groups include: Friday Afternoon Encounters to discuss recent data, the Immunology Club, the Apoptosis and Cell Survival meetings (2x per month) and the weekly Prostate Cancer Group Meetings at LSU; the weekly Breast/Ovarian Group Meeting and the weekly Stem Cells and Cancer Group Meeting at Tulane Cancer Center. The two DOD programs at Xavier have also established a bi-weekly Cancer research Discussion group where faculty involved in DOD projects rotate presenting about the latest status of their project. Tulane mentors and collaborators as well as students are invited to these meetings and this program has been very helpful in bringing our group together.

H. Hold annual workshop, open to all in the Xavier University and Tulane communities, for all PC participants to present results of the preceding year. Faculty, students, and staff will attend and at least one person from each group will present a talk; students will present posters (Months 12, 24, 36)

Our attempts to hold a Cancer Research symposia at Xavier have been foiled by scheduling conflicts with university and department events. We will continue trying to develop a seminar series at Xavier as well as a mini-symposia at with poster sessions. It should be noted that all Xavier students involved in the DOD programs at Xavier present at the universities annual Festival of Scholars in April.

We have established a monthly Cancer Research lunch meeting at Xavier where the faculty involved in our DOD Cancer programs rotate in giving "work in progress" presentations to the group. These meetings are held on a Monday at noon each month and are well attended by all members of the labs involved and our Tulane mentors-collaborators also attend. These meetings have not only assisted Xavier faculty with their projects, but have also provided a place where we can all see what each other are doing. Other Xavier faculty interested in cancer research are now attending these meetings and we may expand these sessions to twice a month. The schedule for these meetings is listed in Appendix 3.

I. Report the activities of the PC program to the presidential-level Tulane-Xavier University Partnership Committee (Months 12, 24, 36)

On September 18, 2006, Dr. Wiese presented a summary and update of all of the Cancer Research programs at Xavier to the university administration, including the president. This type of presentation will be a yearly event from now on at Xavier. Xavier president Dr. Norman Francis has frequently expressed enthusiasm for building cancer research programs at Xavier and he has been a board member of the LCRC for the last two years. The result of this meeting was great enthusiasm from the president to the deans and associate deans to capitalize on existing cancer research programs. Specific areas of interest were obtaining additional funding for research, building cancer related courses and student experiences and hiring faculty with cancer research interest.

J. Ad-hoc committee will explore feasibility of academic course on cancer biology or cancer chemistry taught jointly by Xavier University and Tulane faculty (Month 13)

A new course “Cancer Biology and Health Disparities” has been developed by Dr. Wiese and other Xavier and Tulane faculty involved in the Xavier-Tulane NCI P20 planning grant. This course is being held for the first time in Spring 2007 and includes Xavier as well as Tulane students and faculty. Plans are to continue this course for presentation each spring semester.

K. Submit competitive grant proposal for renewal and expansion of Xavier University-Tulane collaboration in PC (Month 24)

The Xavier-Tulane NCI P20 Planning grant was submitted in February 2005 and the program started during the Katrina evacuation in October 2005.

KEY RESEARCH ACCOMPLISHMENTS

- The program has recovered from Hurricane Katrina and research projects are back to normal operation.
- One additional research project was established in the program for a total of three
- Project #1 Demonstrated that the wild-type p53 inhibits NF- κ B activation by an average of 40 % in the absence of TNF-alpha, the endogenous NF- κ B inducer (Ireland/Abdel-Mageed)
- Project #1 Demonstrated that NF- κ B inhibits p53 in PC-3 and DU-145 cells (Ireland/Abdel-Mageed)
- In Project #2, Pharmacophore models have been made to define the structure requirements of ErbB2 inhibitors (Stevens/Jones)
- In Project #2, Homology model of ErbB2 has been made and used to identify 100 compounds to be screened for antagonist activity (Stevens/Jones)
- A Cancer Biology and health Disparities course has been established by the NCI P20 grant that is a “spin off” of this DOD program. This course involves Xavier and Tulane students and faculty.

REPORTABLE OUTCOMES

- 2 Poster presentations at national meetings
- Involvement of 5 Xavier students in three research projects
- Program members involved in developing a Xavier-Tulane NCI P20 planning grant.
- Established a monthly Cancer Research lunch meeting at Xavier.
- Xavier has hired Dr. Duane E. Johnson, a funded cancer researcher that has a focus on health disparities research.

CONCLUSIONS

The prostate cancer research program started in Y1 continues with the addition of one more Xavier-Tulane collaborative pair and the hire of one new African American faculty with cancer research funding. This program was severely impacted by Hurricane Katrina in 2005 by loss of supplies and loss of time. However, through the efforts of the program participants, the administrations of both Xavier has recovered and Tulane and now with the award of one additional year of funding from the DOD, this program has a good chance for success. The two primary research projects in the program have making good progress, presenting their work and preparing manuscripts. The one additional project added in 2005 is now underway and Xavier students are involved in this project. Xavier has hired cancer researcher Dr. Duane E. Johnson who bring funded research to the small group of cancer researchers established by the Xavier DOD programs. The 6 Xavier faculty involved in both Xavier DOD programs continue to work closely with each other and administrative support is provided by Dr. Wiese as PI of both programs. A monthly cancer research lunch seminar series has been established for both programs and this has become a central point in communicating about our projects to peers, mentors and collaborators. Some faculty involved in the Xavier DOD programs are also involved in the NCI P20 planning grant awarded to Xavier and Tulane in October 2005.

REFERENCES

None

APPENDICES

A-1. CV of Dr. Padma Sankar, new research associate in the Ireland/Abdel-Mageed project

Appendix 1

Padmavathy G. Sankar, Ph.D. {P. S. Naidu}

P.O. Box: 752066

Dayton

OH 45475-2066

Phone: (440)-915-6116

Email: pgurusankar@yahoo.com

KNOWLEDGE/SKILLS/ABILITIES/STRENGTHS:

Managing projects; solving technical issues; extensive educational and research background in biological sciences; molecular biology, cell biology, biochemistry and bioinformatics. Hands on experience in purifying and characterizing macromolecules and knowledge in database soft wares.

EDUCATIONAL QUALIFICATIONS:

PhD [Biology], 1986, Madurai Kamaraj University, India. "Molecular basis of differentiation in *Bacillus*: On the correlation of polymyxin synthesis and sporulation in *Bacillus polymyxa* 2459: A comparative study of the high and low polymyxin producing strains".

TECHNICAL SKILLS:

Recombinant DNA techniques

Gene expression in Prokaryotes and Eukaryotes, single strand and double strand DNA sequencing, promoter analysis, DNA/RNA labeling, full-length cDNA construction using RT-PCR and 5'/3' RACE, cell-free protein expression using *in vitro* transcription and translation techniques, EMSA.

Protein chemistry and engineering

- **Engineering of novel proteins by site-directed and random mutagenesis, structure-function analysis, receptor-ligand interaction studies, protein purification and characterization for quality management (SDS-PAGE, Analytical HPLC, N-terminal amino acid sequencing, peptide mapping, biological activity assays), IEF (isoelectric focusing), assay development, protein labeling, ELISA, and immuno-precipitation.**

Cell Biology techniques

- **Construction and screening for stable cell-lines, transient expression of genes in mammalian cell-lines, immuno-staining of cells and analyzing with immunofluorescence, confocal microscopy, cell-signaling and phosphorylation studies.**

Bioinformatics

Multiple alignments of DNA and protein sequences, identifying protein motifs and putative phosphorylation sites, locating intron / exon boundary sequences and identification of putative regulatory proteins binding regions on promoter sequences.

PROFESSIONAL EXPERIENCE:

2002-2003: Senior Research Associate, Case Western Reserve University, Dept of Research. Investigated the role of poly(ADP-ribose)Polymerase-1 in Ap-2 α mediated transcriptional activation. From this research, we found that the role of PARP-1 in Ap-2 α transcription is dualistic with opposing effects. Separate regions of PARP-1 interact with Ap-2 α and independently control its activation. The catalytic C-terminal domain interacts strongly with Ap-2 α and the middle auto- modification domain interacts with low

affinity, but enhances Ap-2 α transcription. The catalytic domain interaction modifies Ap-2 α with the addition of poly(ADP-ribose) moieties, which in turn affects Ap-2 α ability to bind at DNA specific sequence to promote transcriptional activation. The PARP-1 inhibitor studies unequivocally confirmed the Ap-2 α modification; inhibition affects its ability to transcribe. Based on the studies we hypothesize that PARP-1 enhances the transcriptional activity of Ap-2 α under normal circumstances, whereas its enzymatic activity is used to shut off the mechanism during unfavorable conditions.

1995-1997: Research Fellow, Medical University of South Carolina, Charleston, SC.

Investigated the role of bradykinin involvement in micro and macro vascular complications, using vascular and mesangial cells. This study elucidated the involvement of intracellular calcium elevation leads to tyrosine phosphorylation of tubulin-associated proteins, such as CaM kinase, c-Jun N-terminal kinases phosphorylation in a time dependent manner. Moreover, as the calmodulin inhibitor inhibited the BK-induced increase in c-fos mRNA levels, indicating that calmodulin is required for BK signaling leading to c-fos induction. These results implicate the calcium-calmodulin pathway in the mechanisms for regulating MAPK activity and the resultant c-fos expression induced by BK.

1992-1994: Visiting Research Associate, Purdue University, West Lafayette, IN.

Studied the cell differentiation with muscle cells as a model system. Concluded that muscle regulatory factors play a significant role in muscle cell differentiation and complement each other functions to an extent. However, the factor MRF4 (abundantly present in adult muscle cells) activation is regulated synergistically by Myogenin and MEF2 factors during muscle cell differentiation.

1987-1992: Research Associate, Michigan State University, East Lansing, MI.

Biodegradation of lignin by *Phanerochaete chrysosporium*: Significance of lignin peroxidase enzymes of *Phanerochaete chrysosporium* in lignin degradation. Studied lignin-peroxidase isozymes' structural, functional arrangement and distribution of the genes, as well as temporal expression of these genes at RNA level.

1986 to 1987: Research Associate, NBTB-UGC collaborative program M.K.University, Madurai, India.

PUBLICATIONS:

1. Li, M., **Naidu, P.**, Yu. Y., Berger, N. A., Kannan, P. (2004). Dual regulation of AP-2 α Transcriptional Activation by poly (ADP-ribose) polymerase-1. *Biochem. J.* 382(Pt1): 323-9.
2. **Naidu, P.S.**, Velarde, V., Kappler CS, Young RC, Mayfield RK, Jaffa AA.(1999). Calcium-calmodulin mediates bradykinin-induced MAPK phosphorylation and c-fos induction in vascular cells. *Am J Physiol.* 277(3 Pt 2): H1061-8.
3. Jaffa, AA, Miller, BS, Rosenzweig, SA, **Naidu, P.S.**, Velarde, V., Mayfield RK. (1997). Bradykinin induces tubulin phosphorylation and nuclear translocation of MAP kinase in mesangial cells. *Am J Physiol.* 273 (6 Pt 2): F916-24.
4. **Naidu, P. S.**, Ludolph, D.C., To, R.Q., Hinterberger, T., Elizabeth T.J. and Konieczny, S. F. (1995). Myogenin and MEF2 function synergistically to activate the MRF4 promoter during Myogenesis. *Mol. Cell. Biol.* 15: 2707-2718.
5. Boominathan, K., D' Souza, T. M., **Naidu, P.S.**, Dosoretz, C. and Reddy, C. A.(1993) Temporal expression of the Major Lignin Peroxidase Genes of *Phanerochaete chrysosporium*. *Appl. Environ. Microbiol.* 59: 3946-3950.
6. **Padmavathy S. Naidu**, Zhang, Y. Z. and Reddy, C. A. (1990). Characterization of a new lignin peroxidase gene [GLG6] from *Phanerochaete chrysosporium*. *Biochem.Biophys.Res. Commun.* 173: 994-1000.

7. **Padmavathy S. Naidu** and Reddy C.A. (1990). Nucleotide sequence of a lignin peroxidase gene GLG3 from white- rot fungus, *Phanerochaete chrysosporium*. Nucleic Acids Res. 18: 7173.
8. **Padmavathy S. Naidu** and Jayaraman K. (1987). Characterization of the membrane bound multienzyme complex involved in polymyxin synthesis in *B. Polymyxa*. International Symposium on Biomembranes: Structure, Biogenesis and Transport 13: 339-345.
9. Balakrishnan, R., Satwant Kaur, Goel, A.K., **Padmavathy S.** and Jayaraman, K. (1980). Biosynthesis of polymyxin by *Bacillus polymyxa* . Part Two: on the nature and interaction of the multienzyme complex with the product polymyxin. Arch.Biochem.Biophys. 200: 45-54.

PAPERS PRESENTED IN INTERNATIONAL AND NATIONAL CONFERENCES:

- American diabetes Association: 56th Annual Meeting June 1996.
Ayad Jaffa, **Padma Naidu**, Bradly Miller, Steven Rosenweig, and Ronald Mayfield:
Bradykinin induces tubulin phosphorylation and MAPkinases nuclear translocation in essential cells.
- American Society for Microbiology, 91st Annual Meeting. May 1992. New Orleans, LA- USA.
Boominathan, K., **Naidu, P.S.**, D' Souza, Reddy, C.A.: Temporal Expression of the Major Lignin Peroxidase genes of *Phanerochaete chrysosporium*.
- American Society for Microbiology, 89th Annual Meeting. May 1990. Anaheim, CA-USA.
Padmavathy S. Naidu, Zhang, Y. Z., and Reddy, C.A.: Cloning and sequencing of New Lignin Peroxidase Gene from White- rot Basidiomycete *Phanerochaete chrysosporium*.
- American Society for Microbiology, 88th Annual Meeting. May 1989. New Orleans, LA- USA.
Padmavathy S. Naidu, Reddy, C.A.: Analysis of nucleotide sequence of a lignin peroxidase gene from White-rot Basidiomycete *Phanerochaete chrysosporium* BKMF- 1767.
- Symposium on Streptomyces. 1987 National Chemical Institute. Pune. India.
Mathumathi, R., **Padmavathy S. Naidu**, and Dharmalingam, K.: Extra-cellular Secretion on *Streptomyces*.

References: Will be provided upon request

Appendix 2

BIOGRAPHICAL SKETCH

Follow this format for each person. **DO NOT EXCEED TWO PAGES.**

NAME: Duane E. Johnson, Ph.D.		POSITION TITLE Assistant Professor	
EDUCATION/TRAINING (<i>Begin with baccalaureate or other initial professional education, such as nursing, and include postdoctoral training.</i>)			
INSTITUTION AND LOCATION	DEGREE (<i>if applicable</i>)	YEAR(S)	FIELD OF STUDY
University of Houston, Houston, Texas	B.S.	1984	Biology
Morehouse College, Atlanta, GA	B.S.	1986	Biology
Texas Southern University, Houston, TX	M.S.	1990	Molecular
Meharry Medical College, Nashville, TN	Ph.D.	1996	Biology/Pha
University of Cincinnati, Ohio and NIOSH	Postdoc. Fellowship	1996-1998	rmacology Pharmacolo gy

Research and Professional Experience:

Assistant Professor, Xavier University of Louisiana, College of Pharmacy, Division of Basic Sciences. Research focus is translational research/ experimental therapeutics in breast and prostate cancer; teaching responsibilities include Pharmacology, Principles of Pharmacology I & II, Introduction to Drug Actions (2/07-present)

Visiting Assistant Professor, University of Nebraska Medical Center, Department of Biochemistry and Molecular Biology. Research focus is translational research/ experimental therapeutics in breast and prostate cancer (1/06-12/06)

Assistant Professor, Dillard University, Departments of Chemistry and Biology and Director of Research for the Division of Natural Sciences and Public Health. Currently teaching Cell and Molecular Biology, General Biology and Pharmacology to students in the Division of Natural Sciences and Public Health, as well as the Division of Nursing. (8/01-12/05)

Director for Research, Dillard University, Division of Natural Science and Public Health. To develop an infrastructure for research in the Division of Natural Sciences and Public Health. Division Administrator, Morehouse College, Division of Science and Mathematics. To manage the Division of Science and Mathematics and the Packard Scholars Program (1/00-7/01)

Research Scientist, Morehouse College, Department of Biology. Conducted research in Experimental Therapeutics in Breast and Prostate Cancer (8/98-7/01)

Assistant Professor, Morris Brown College, Department of Chemistry. Instructor of Basic Pharmacology, Chemistry, and Research Experimental Therapeutics, and drug development of anticancer agents against various breast and prostate cancers (8/98-present)

Post Doctoral Fellow, University of Cincinnati, Department of Molecular Pharmacology. Examined the relationship between DNA adduct promoting agents and tumorigenesis (12/97-8/98)

Post Doctoral Fellow, University of Cincinnati, Department of Physiology. Examined the relationships between myocardial contractions and heart compensatory mechanisms as it relates to the prevention of cardiovascular disease (9/97-12/97)

Post Doctoral Fellow, Visiting Scholar Resident Program, National Institute for Occupational Safety and Health (NIOSH). Examined tumor promotion in breast cancer models (12/96-7/97).

Lecturer, Cincinnati State Technical and Community College. Taught pharmacology to technical students in the fields of medical technology, nursing, respiratory therapy, and surgical technology (6/97-8/97).

- **Sabbatical Internship, Marian Merrell Dow Pharmaceuticals.** Participated in drug discovery of compounds that I synthesized; techniques included tumor implantations, drug dosing of animals, tumor measurements, necropsies of tumor implanted animals, animal toxicity studies, estrogen receptor binding assay, tyrosine receptor binding assay, estrogen receptor immunoassay, DNA mobility shift assay, androgen receptor binding assay, flow cytometry experiments, apoptosis experiments, image analysis of MCF-7 cells, CDK4 assay (7/95-11/95)

B. PUBLICATIONS:

The combination of Cox-2 and EGF serve as potential prognostic biomarkers for hormone refractory prostate cancer.

¹K. Parker-Johnson, ²N.L. Emmett, ³A.L. DePass, ⁴W. Rayford, ¹J.D. Daigle, ⁵B.A. Jackson, and ¹D. E. Johnson. ¹*Dillard University, Department of Biology, New Orleans, LA 70122*; ²*Morehouse School of Medicine, Department of Physiology, Atlanta, GA30310*; ³*Long Island University, Brooklyn, NY*; ⁴*LSU Health Sciences Center, New Orleans, LA, 70112*; ⁵*Boston University, Department of Biochemistry, Boston, MA 02118, Proceedings of AACR, Volume 44, April 2005.*

Novel DJ56 Causes Tumor Reduction in ER+ Breast Cancer Cells.

Tiffany Griffin, Byron Knowles, K. Parker-Johnson, Emory Minnard, N.L. Emmett, D.E. Johnson, Proceedings of AACR Volume 44, April 2005.

Novel DJ Compounds Significantly Decrease the Expression of Transforming Growth Factor Beta-3 Gene in Human Prostate Cancer Cell Line LNCaP using Microarray. **Jeremy D. Daigle, KiTani A. Parker-Johnson, Courtney White, Guoshen Wang, Nerimiah L. Emmett, Walter Rayford, Duane E. Johnson. Abstract # 1713, Proceedings of the AACR, Volume 45, March 2004.**

cDNA Micro Array Analysis Reveal Prostaglandin Pathway as Target for Novel DJ Compounds During Antiproliferation of Human Prostate Cancer Cells. **KiTani A. Parker-Johnson, Bruce A. Jackson, Jeremy D. Daigle, Guoshen Wang, Nerimiah L. Emmett, Walter Rayford, Duane E. Johnson. Abstract # 1664, Proceedings of the AACR, Volume 45, March 2004.**

Novel Isochalcone DJ52A Increases Expression of NER and Apoptotic Genes Using Microarray Analysis. **KiTani Parker-Johnson, Nerimah L. Emmet, David B. Cooke, Walter Rayford, and Duane E. Johnson. Abstract #2682, Proceedings of the AACR, Volume 44, 2nd ed., July 2003.**

"Alpha, beta, unsaturated ketones demonstrate antiproliferative activity against African American Breast Cancer cells", 19th annual San Antonio Breast Cancer Symposium, December 1999. P. E. Campbell, K. P. Johnson, D. B. Cooke III, and D. E. Johnson.

DJ52 proves to be more potent than tamoxifen against human breast cancer cell line

MCF-7, 19th annual San Antonio Breast Cancer Symposium, December 1999. B. O. Guillory, K. P. Johnson, D. B. Cooke III, and D. E. Johnson.

"The inhibitory effects of a dopamine agonist SKF38393 on MCF-7 cells",Anticancer Drug, vol. 6, June 1995. **D. E. Johnson, J. Ochieng, S. L. Evans.**

"Antiproliferative activity of Phenyl acetic acid derivatives against MCF-7cells", vol 7, May 1996 Anticancer Drugs, **D. E. Johnson, J. Ochieng, S. L. Evans.**

PROFESSIONAL ORGANIZATIONS

American Association for Cancer Research, American Society for Clinical Oncology

GRANTS

2006-2007, Susan G. Komen Research Grant, 2004- HBCU-UPS, 2003 Board of Reagents grant, 2003 Arthur Vinning Davis Grant, 2003 RIMES grant-NSF, Morehouse School of Medicine/ University of Alabama Cancer Partnership U-56 Grant, 2000 Center for Disease Control (CDC) Supplement, NIH/NCI University of Michigan Cancer Consortium Supplement 2000, 1999-National Institute of Environmental Health and Science Award, 1997-98 NIH Molecular Pharmacology Training Grant, 1996-97 Visiting Scientist Research Program Training grant, 1992-95 Minority Research Center of Excellence grant (MRCE).

Honors and activities

Excellence in Research 2004- 2005, AACR-HBCU Faculty Scholar in Cancer Research Award 1999-2001, American Society for Cell Biology Faculty Award 2002-03.

Other

Patent pending on certain compounds

Research Focus

Experimental Therapeutics in Breast and Prostate Cancer with a focus on Health Disparity

The main focus of this laboratory is to identify molecular and genetic biomarkers that might serve as key cellular targets for design of strategic pharmacological agents that may be used to treat various types of metastatic breast and prostate cancers. In an attempt to uncover these biomarkers, our approach uses the strategy of drug design studies, pharmacological screening, molecular biology techniques, including microarray analysis, and animal tumor studies. An important objective of this lab is the use of various types of models from different ethnic backgrounds to examine the pharmacogenetic differences in their responses to different treatment modalities. It is the ultimate vision for this laboratory to gain a better understanding of the differences between the etiologies of breast and prostate cancers that originate from African Americans vs. other ethnic backgrounds.

Appendix 3

**Department of Defense
Congressionally Directed Medical Research Programs at
Xavier University of Louisiana**

Breast Cancer and Prostate Cancer Research

Noon – 1:00pm

Monthly Research Meeting Schedule

Date:	Presenters
Monday September 7, 2006	Agenda: Status of Xavier DOD HBCU/MI Prostate Cancer and Breast Cancer Training
Attendees: David Wolfgang, Charles Miller, Guandi Wang, Matt Burow, Thomas Wiese, Asim Abdel-Mageed, Suresh Sikka, Steven Hill, Shubha Ireland, Cheryl Stevens, Dr. Shankar, Stephanie Colbert	
Monday October 16, 2006	Wiese-Hill Project
Attendees: David Wolfgang, Guandi Wang, Shubha Ireland, Matt Burow, Thomas Wiese, Asim Abdel-Mageed, Steven Hill, Cheryl Stevens, Dr. Shankar, Chris Segar, W. Ming, Maryam Foroozesh, Stephanie Colbert	
Monday November 6, 2006	Wang-Burow Project
Attendees: David Wolfgang, Guandi Wang, Matt Burow, Thomas Wiese, Asim Abdel-Mageed, Steven Hill, Cheryl Stevens, Dr. Shankar, Chris Segar, W. Ming, Maryam Foroozesh, Stephanie Colbert	
Monday December 4, 2006	Steven-Jones Project
Attendees: David Wolfgang, Guandi Wang, Thomas Wiese, Frank Jones, Cheryl Stevens, Dr. Shankar, Chris Segar, W. Ming, Maryam Foroozesh, Stephanie Colbert, Dr. Wang's lab tech	
Monday February 5, 2007	Wiese-Hill Project
Attendees: Suresh Sikka, Steven Hill, Abdel Mageed, Shubha Ireland, Chris Segar, Kirk Williams, Cheryl Stevens, Maryam Foroozesh, Gurandi Wang, David Wolfgang, 3 lab techs, Thomas Wiese, Stephanie Colbert	
Monday March 26, 2007	Ireland-Mageed Project
Attendees:	
Monday April 30, 2007	Wolfgang-Miller Project
Attendees:	